REMARKS

This Amendment is in response to the Examiner's Office Action mailed on July 20, 2004. Claims 1-21, 23-25 and 28-42 have been canceled. Claims 22, 26 and 27 have been amended. Claims 22, 26, 27, and 43-46 are now pending. Reconsideration of the application is respectfully requested in view of the above amendments to the claims and the following remarks. For the Examiner's convenience and reference, Applicants' remarks are presented in the order in which the corresponding issues were raised in the Office Action.

I. Rejections under 35 U.S.C. § 112, Second Paragraph

The Examiner rejects claims 22, 24-31, 43-46 under 35 U.S.C. § 112, Second Paragraph as being indefinite. Applicants amend independent claim 22 to specify that the method is used to determine whether the amplified product comprises nucleic acid encoding SHBsAg having a mutation at amino acid position 130 from glycine to aspartic acid, or at amino acid position 131 from threonine to asparagine. Dependent claims 26 and 27 have been amended accordingly. Claim 31 has been canceled. In view of these amendments to the claims, Applicants submit that the pending claims are definite to one of ordinary skill in the art and respectfully request the withdrawal of the rejection under 35 U.S.C. § 112, Second Paragraph.

II. Rejections under 35 U.S.C. § 103(a)

1) Rejection of claims 22 and 24-31

The Examiner rejects claims 22 and 24-31 under 35 U.S.C. § 103(a) as being unpatentable over Weinberger *et al.* in view of Mbayed *et al.* and further in view of Kohno *et al.* (1996) (J. General Virology 77:1825-1831) and Ho *et al.* (1998) (J. Biomed. Sci. 5:355-362).

Independent claim 22 as amended specifies a method for detecting a HBV variant that may have escaped immunological detection of HBV surface antigen (HBsAg). In particular, the method is used to determine whether the amplified product comprises nucleic acid encoding SHBsAg having a mutation at amino acid position 130 from glycine to aspartic acid, or at amino acid position 131 from threonine to asparagine. Support for the amended claim language appears

in the Specification, for example, on page 31, EXAMPLE 1, lines 27-35; and in Table 2 on page 33.

As acknowledged by the Examiner, Weinberger et al. does not specifically teach using primers of SEQ ID NOs: 1 and 2 to detect HBV variants. Neither does Mbayed *et al.* Further neither Weinberger *et al.* nor Mbayed *et al.* teaches or suggests using the primers of SEQ ID NOs: 1 and 2 to detect HBV strains that may have escaped immunological detection of the HBV surface antigen (HBsAg), i.e., HBV strains tested negative for HBsAg. Moreover, none of the references teaches or suggests detecting the HBV strains through detection of a mutation in major HBV surface antigen (SHBsAg) at amino acid position 130 from glycine to aspartic acid, or at amino acid position 131 from threonine to asparagine.

The new references cited by the Examiner, Kohno *et al.* (1996) and Ho *et al.*, each alone or in combination with Weinberger *et al.* and Mbayed *et al.*, also fail to teach or suggest the claimed invention. As acknowledged by the Examiner, Kohno *et al.* teaches a mutation of HBsAg at amino acid position 130 from glycine to asparagine; and Ho *et al.* a mutation of HBsAg at amino acid position 145 to Arginine, 133 to threonine, and 131 to isoleucine.

In view of the failure of the cited references to teach or suggest the claimed invention, Applicants submit that a prima facie case of obviousness has not been established under 35 U.S.C. § 103(a). Withdrawal of this ground of rejection is respectively requested.

2) Rejection of claim 43

The Examiner rejects claim 43 under 35 U.S.C. § 103(a) as being unpatentable over Weinberger et al. in view of Mbayed *et al.* and Ho *et al.*, and further in view of Mason *et al.*

As discussed in detail above, independent claim 22 as amended specifies a method for detecting a HBV strain that may have escape immunlogical detection of HBsAg through detection of a mutation in SHBsAg at amino acid position 130 from glycine to aspartic acid, or at amino acid position 131 from threonine to asparagine.

None of Weinberger et al., Mbayed *et al.* and Ho *et al.* teaches or suggests the claimed invention. Mason et al. merely teaches reverse transcribing HBV RNA.

Thus, the cited references, each alone or in combination, fail to teach or suggest the claimed method. Claim 43 is therefore not only novel but also non-obvious under 35 U.S.C. § 103(a).

3) Rejection of claims 44-46

The Examiner rejects claims 44-46 under 35 U.S.C. § 103(a) as being unpatentable over Weinberger et al. in view of Mbayed *et al.* and further in view of Kohno *et al.* and Ho *et al.* and further in view of Dattagupta *et al.*

As discussed in detail above, independent claim 22 as amended specifies a method for detecting a HBV strain that may have escape immunlogical detection of HBsAg through detection of a mutation in SHBsAg at amino acid position 130 from glycine to aspartic acid, or at amino acid position 131 from threonine to asparagine.

None of Weinberger et al., Mbayed *et al.,* Kohno *et al.* and Ho *et al.* teaches or suggests the claimed invention. Mason *et al.* merely teaches immobilizing amplification primers on a substrate.

Thus, the cited references, each alone or in combination, fail to teach or suggest the claimed method. Claim44-46 are therefore not only novel but also non-obvious under 35 U.S.C. § 103(a).

CONCLUSION

Applicants earnestly believe that they are entitled to a letters patent, and respectfully solicit Examiner to expedite prosecution of this patent application to issuance. Should Examiner have any questions, the Examiner is encouraged to telephone the undersigned.

Respectfully submitted,

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